

What is claimed is:

1.

A method of producing a heterologous protein in fungi comprising:
providing a recipient fungi cell wherein the quality control mechanism in said cell is modified so that incompletely folded heterologous proteins are not degraded in the endoplasmic reticulum; and
introducing to said recipient fungi cell a polynucleotide expression construct.

2.

The method of claim 1 wherein said fungi cell is a yeast cell.

3.

The method of claim 1 wherein said introducing is by a transformation method selected from the group consisting of: PEG, electroporation, particle bombardment, and LiAc.

4.

The method of claim 3 wherein said transformation method is LiAc mediated transformation.

5.

The method of claim 1 wherein said polynucleotide construct is within a yeast based plasmid.

6.

The method of claim 1 wherein said recipient cell is modified so that O-glycosylation is inhibited.

7.

The method of claim 6 wherein said recipient cell comprises inhibition of a protein mannosyltransferase gene.

8.

The method of claim 7 wherein said mannosyltransferase gene comprises a gene selected from the group consisting of PMT 1, PMT 2, PMT 3, PMT 4, PMT 5, AND PMT 6.

9.

The method of claim 8 wherein said PMT gene is PMT 1.

10.

The method of claim 8 wherein said PMT gene is PMT 2.

11.

The method of claim 8 wherein said recipient gene provides inhibition of a Bypass of Sec Thirteen gene.

12.

The method of claim 11 wherein said Bypass of Sec Thirteen gene is BST1.

13.

A yeast cell transformed by the method of claim 1.

14.

A protein produced by the method of claim 1.

15.

A method of producing a heterologous protein in a fungi cell comprising:
providing a recipient fungi cell wherein o-glycosylation is inhibited so that misfolded heterologous proteins are not degraded; and
introducing to said recipient fungi cell a polynucleotide expression construct, said construct comprising a structural gene to be expressed in said cell, said gene operably linked to control sequences for expression in a fungi cell wherein said recipient fungi cell.

16.

The method of claim 15 wherein said fungi cell is a yeast cell.

17.

The method of claim 15 wherein said introducing is by a transformation method selected from the group consisting of: PEG, electroporation, particle bombardment, and LiAc.

18.

The method of claim 17 wherein said transformation method is LiAc mediated transformation.

19.

The method of claim 15 wherein said polynucleotide construct is within a yeast based plasmid.

20.

The method of claim 15 wherein said recipient cell comprises a protein mannosyltransferase gene the expression of which is inhibited.

21.

The method of claim 20 wherein said mannosyltransferase gene comprises a gene selected from the group consisting of PMT 1, PMT 2, PMT 3, PMT 4, PMT 5, AND PMT 6.

22.

The method of claim 15 wherein said PMT gene is PMT 1.

23.

The method of claim 15 wherein said PMT gene is PMT 2.

24.

A yeast cell transformed by the method of claim 15.

25.

A protein produced by the method of claim 15.

26.

A method of producing a heterologous protein in fungi comprising:

providing a recipient fungi cell wherein Bypass of Sec

Thirteen expression is inhibited so that misfolded heterologous proteins are not degraded; and

introducing to said recipient fungi cell a polynucleotide expression construct, said construct comprising a structural gene to be expressed in said cell, said gene operably linked to control sequences for expression in a fungi cell wherein said recipient fungi cell.

27.

The method of claim 1 wherein said fungi cell is a yeast cell.

28.

The method of claim 1 wherein said introducing is by a transformation method selected from the group consisting of: PEG, electroporation, particle bombardment, and LiAc.

29.

The method of claim 28 wherein said transformation method is LiAc mediated transformation.

30.

The method of claim 28 wherein said polynucleotide construct is within a yeast based plasmid.

31.

The method of claim 28 wherein said Bypass of Sec Thirteen gene is BST1.

32.

A yeast cell transformed by the method of claim 28.

33.

A protein produced by the method of claim 28.

34.

A polynucleotide useful for transforming yeast cells comprising:

A promoter capable of driving expression in a yeast cell

A bacterial replicon for propagation in E. Coli,

A transcription termination signal;

A yeast BiP signal sequence;

A yeast origin and centromere for replication and mitotic stability, wherein said polynucleotide directs expression of the recombinant protein to the SRP pathway.

35.

The polynucleotide of claim 34 further comprising a 6-histidine tag to facilitate protein purification.

36.

The polynucleotide of claim 34 wherein the vector is as depicted in Figure 14.

37.

A yeast cell for production of heterologous proteins, said cell comprising a modification so that a quality control mechanism in said cell is modified so that misfolded heterologous proteins are not degraded in the endoplasmic reticulum.

38.

The yeast cell of claim 37 wherein said modification comprises a modification that inhibits of O-linked glycosylation.

39.

The yeast cell of claim 38 wherein said modification is a PMT loss of function modification.

40.

The yeast cell of claim 39 wherein said PMT modification is to PMT 1.

41.

The yeast cell of claim 41 wherein said PMT modification is to PMT 2

42.

The yeast strain of claim 37 wherein said modification comprises a modification that inhibits the production of Bypass of Sec Thirteen.